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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/380,324	12/08/99	CICHUTEK K	10383/006001

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EXAMINER	
BRUNOVSKIS,P	
ART UNIT	**PAPER NUMBER**
1632	15

DATE MAILED: 12/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/380,324	Cichutek And Stitz
Examiner	**Group Art Unit**
Peter Brunovskis	1632

☒ Responsive to communication(s) filed on *Sep 13, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *13-27* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *9*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The response filed 9/13/00 (Paper No. 12) has been entered. Entry of new claims 13-31 and cancellation of claims 1-12 is acknowledged. Claims 13-31 are pending in the instant application. Applicant's arguments filed 9/13/00 have been fully considered and will only be considered to the extent that they apply to newly claimed subject matter; arguments directed to any other subject matter is considered moot.

Priority

The certified translation of Application No. 19707971.7 filed 9/13/00 (Paper No. 13) has been entered.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. Any response to this Office Action which fails to meet *all of these requirements*

will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Objections

Claims 13, 17, 21, 23, 25, and 26 are objected to because of the following informalities: In line 3 of claim 13, the comma between "virus envelope" and "comprising" should be removed and inserted after "envelope protein" (also line 3) instead. In claim 17, "*gag*-genes" and "*pol*-genes" (plural) should be changed to --*gag*-gene-- and --*pol*-gene-- (singular). In claim 21, "Packaging cells" should be changed to --The packaging cells--. In claims 23 and 25, "wherein the specific cell type is CD4-positive cells" should be changed to 1.--wherein the specific cell type is a CD4-positive cell--. In claim 26, "wherein the CD4-positive cells are" should be changed to --wherein the CD4-positive cell is a human cell--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 (and dependent claims) is indefinite in its recitation of "a virus envelope, comprising a full-length surface envelope protein" since it is not clear whether this full-length surface envelope protein is from HIV or SIV or whether it can come from any non-HIV/SIV virus comprising a viral envelope.

Claim 14 (and dependent claims) is indefinite in its recitation of the phrase "wherein the transmembrane envelope protein....is a truncated variant" since it is unclear how "truncated variant" is defined in this context or the limitation distinguishes itself from a "truncated transmembrane envelope protein" (or further limits it).

Claim 15 is indefinite in its recitation of the phrase, "wherein the...and the...are each independently, a...., or ..., surface envelope or transmembrane envelope protein" since it is unclear what is meant by "are each independently" in the context of the phrase or what structural limitations apply to the claim. The claim is extremely worded, particularly since it starts out with "wherein the full-length surface envelope protein and the transmembrane envelope protein" and concludes with ", surface envelope or transmembrane envelope protein" without making clear how these terms are connected by the intervening part.

Claim 16 recites the limitation "any other fragment of the transmembrane envelope protein of a murine leukemia virus" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 is indefinite in its recitation of the phrase, "is modified by fusion to the C-terminus" since it is not clear as to what "C-terminus" is directed or what is meant by "modified" in the context of fusion to the "C-terminus" or "to any other fragment..." or of any other retrovirus". Applicants claim to have overcome the indefiniteness rejection as previously applied to claim 3 in their amendment of claim 16; however, this is not persuasive since they have merely incorporated the phrase "wherein the truncated variant of the transmembrane envelope protein is modified by fusion to the C-terminus or ...." without addressing the problems raised once more above. Presently it is not clear what structural relationship exists between the truncated variant and the "modifi[cation] by fusion to the C-terminus" (of what?).

Claim 17 recites the limitation "the transfected packaging cell" in line 9. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 (and dependent claims) is indefinite in its recitation of the term "psi-negative expression construct" since this term is not defined in the specification and since the specification explicitly teaches that "the expression construct has to contain the packaging signal 'psi'" (p. 1, line 24).

Claims 17 and 18 (and dependent claims) are indefinite because the method steps do not relate back to their preambles which recite "method[s] for preparing packaging cells" but rather

appear to refer to methods for producing retroviral vectors. Additionally, the claims are indefinite in their recitation of the phrase "to be transferred" since it is unclear how this is related to methods for preparing packaging cells, how the term "transferred" is defined in context, or what it is directed to. Further, since it is not clear what defines the metes and bounds of "packaging cells" as set forth in claim 17, it is not possible evaluate the metes and bound of "packaging cells" as set forth in claim 21.

Claim 20 is indefinite in its recitation of the term "the expression construct" because it is unclear how the term "expression construct" in claim 17 is defined in the context of the claim or what it is directed to. Claim 17 only recites "expression construct[s]" in the context of "psi-negative expression construct[s] comprising the gag-genes and the pol-genes of murine leukemia virus (MLV)" or "psi-positive expression construct[s] encoding a desired gene product to be transferred". Claim 17 only refers to envelope[s] in the context of "transcriptional cassette[s]".

Claim 22 (and dependent claims) is indefinite in its recitation of the phrase "further comprising a therapeutic or reporter gene or fragment thereof" since it is unclear how "therapeutic" and "fragment thereof" are defined, what their metes and bounds are, or what "fragment thereof" is directed to. For example, it is not clear whether "a therapeutic" is meant to be limited to "a therapeutic gene" or whether it also embraces therapeutic *compounds*, for example.

Claims 24 and 30 (and dependent claims) are indefinite in its recitation of the phrase "inserting into the retroviral vector an mRNA" since it is unclear how this step is performed,

inasmuch mRNAs are not typically known to be "inserted into retroviral vectors". The claim is also indefinite in its recitation of "the retroviral vector" in line 5 since it is not clear which retroviral vector (the one in line 3 or the one in line 4 after insertion of the mRNA?) is being referred to.

Claims 29 and 31 are indefinite in its recitation of "active agent" in line 2 since it is not clear what is meant by this term in the context of the claim or the claim is patentably distinguishable from claims 23 and 28.

Claim 30 is indefinite in its recitation of the phrase "HIV-inhibiting gene or a fragment thereof" since it is not clear how this term is defined or what its metes and bounds are.

Claim 30 recites the limitation "the foreign gene" in lines 6-7. There is insufficient antecedent basis for this limitation in the claim. Further, as presently recited, the claim does not provide for transfer of the "fragment thereof" in the final transfection step.

Claim 31 is indefinite since it does not provide for transfer of "a fragment thereof" in the final transfection step and because it is unclear whether "active agent" is directed to "fragment thereof" only or to the "fragment thereof" *and* the "foreign gene".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-16 and 22-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13, 15 and 22-31 recite compositions and methods comprising a retroviral vector comprising a full-length surface envelope protein from any retrovirus other than HIV or SIV, nor is there any evidence indicating that Applicants contemplated or were in possession of retroviral vector comprising *full-length* truncated transmembrane envelope proteins of HIV or SIV. In addition, the response, filed 9/13/00 fails to indicate which sections of the specification provide support for the newly claimed subject matter. The specification does not provide support in the specification for embodiments containing full-length transmembrane envelope proteins of HIV or SIV; in fact the specification explicitly teaches against such use. For example, the specification teaches that only "*env* gene variants [i.e. SIV] displaying a intracellular domain of no more than 19 amino acid moieties resulted in the generation of pseudotyped MLV-vectors successfully transducing T-cells [and that] [t]he variants *wt env* and 36 *Δenv* did not generate detectable amounts of these vectors" (p. 16, lines 1-4). Additionally, the inventors own work (e.g. Schnierle et al., Proc. Natl. Acad. Sci. USA, 94:8640-8645, 1997) and the teachings relied upon in the response of 9/13/00 (i.e. Lodge), contradict the notion of making pseudotypic MLV/HIV vectors comprising full-length transmembrane envelopes from HIV and explicitly teach against it.

Further, claims 22 and 24 recite compositions comprising pseudotypic retroviral vectors that can mediate transfer of genetic and/or therapeutic material into "a specific cell type"; claims 23 and 25 appear to further limit the "specific cell type" to a mammalian CD4-positive cell. However, there is no evidence or record indicating that Applicants contemplated or were in possession of retroviral vectors capable of mediating transfer of genetic and/or therapeutic material into any cells other than CD4-positive mammalian cells. Since there is no basis identified for incorporating the new matter described above, it is rejected under 35 U.S.C. 112, first paragraph. See *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

Claims 13 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pseudotypic retroviral vectors comprising MLV cores, full-length HIV or SIV surface envelope proteins and truncated HIV or SIV transmembrane envelope proteins mediated transfer into CD4-positive mammalian cells, does not reasonably provide enablement for retroviral vectors comprising *full-length* transmembrane envelopes from HIV or SIV mediating transfer into *any other* "specific cell type". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As described above, the specification teaches that only "*env* gene variants displaying a intracellular domain of no more than 19 amino acid moieties resulted in the generation of pseudotyped MLV-vectors successfully transducing T-cells [and that] [t]he variants *wt env* and 36 *Δenv* did not generate detectable

amounts of these vectors" (p. 16, lines 1-4). Further, previous attempts by others in the prior art to create pseudotypic MLV/HIV have been unsuccessful (Wilson et al., J. Virol., 63(5):2374-2378, 5/89). Neither the examples, nor the prior art provides a basis for making pseudotypic retroviral vectors comprising full length transmembrane envelopes from HIV or SIV. In addition, the specification does not provide any guidance or reasonable expectation of success for making such vectors, particularly in view of the previous unsuccessful efforts. Moreover, the specification does not provide a basis for targeting any specific cell type apart from mammalian CD4+ cells or teach any other specific cell types that can be targeted using the vectors of the instant invention. In view of the lack of success in making pseudotypic retroviral vectors comprising full length transmembrane envelopes from HIV or SIV, and the lack of guidance for overcoming prior problems in the art and for targeting specific cell types apart from CD4+ mammalian cells, the specification fails to provide an enabling disclosure for the subject matter in the rejected claims.

Claims 19, 20, 22, 23, 29, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth against prior claims 6, 7, and 9-12 in the Office Action of 3/9/00 as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejected claims recite or require cell lines (TELCeB6) and expression plasmids (pLβAc/env-Tr712-neo and pMB2) that are encompassed by the definitions for biological material set forth in 37 C.F.R. 1.801. Applicant's arguments filed 9/13/00 have been fully considered but they are not persuasive. Applicants submit that the construction of the packaging cell line TelCeB6 is described in Cosset et al. However, there is no evidence of record to suggest either that this cell line is readily available to the public or that it is obtainable by a reproducible method set forth in the specification. Indeed, Applicants rely on information (i.e. Cosset) inappropriately incorporated by reference. Secondly, one of skill in the art would readily recognize that no two stably-transformed cell lines are identical or reproducible. Although one could follow the approach set forth in a prior art reference to generate an analogous cell line functioning in a similar manner, apart from determining the precise nature of the integrations in TelCeB6 and employing a different methodology than that set forth in Cosset, one could not reproduce the TelCeB6 in the absence of undue experimentation. Similarly, the same arguments apply to the expression constructs set forth in claim 20 inasmuch as the evidence of record fails to suggest that any of the recited plasmids are readily available to the public or obtainable by a reproducible method set forth in the specification.

To the extent that claims 22, 23, and 29 are drawn to vector compositions comprising therapeutic genes for in vivo administration to mediate expression in a cell of an "active [pharmaceutical] agent", along with claims 30 and 31, these claims are drawn to methods of gene therapy that are not enabled by the instant disclosure. The specification does not provide any

utility other than gene therapy for using retroviral compositions comprising the intended use limitations of "therapeutic gene" or "express[ing] [an] active agent". Applicants submit that "those skilled in the art would know *from the prior art* how to use the vectors of the present invention for gene therapy" (emphasis added). However, since gene therapy was not routinely performed at the time the invention was made, it is imperative that Applicants *specification*--not the prior art--provide a basis for establishing that they have overcome the problems in the art and further provide specific guidance on how to use the vectors of the instant invention to treat disease. While Applicants claim to have addressed the "so-called Achilles heel of gene therapy", gene delivery, they provide no evidence of targeted in vivo delivery in CD4+ positive cells. They further state that "[b]ased on the date in the application and as described in the Lodge paper, applicants submit that the use of the new retroviral vectors for gene therapy is enabled and that successful results are predictable" and that "those of skill in this field would expect that the new retroviral vectors would also work ex vivo and in vivo" (p. 10). First, the various statements invoking the results of Lodge bear no probative value in overcoming the prima facie case against enablement--what matters is the guidance provided in the instant specification. Although the claimed invention purports to addresses *at least one of problems plaguing gene therapy--targeting*--it does *not*, for example, address other problems concerning persistence of expression, immunogenicity, or targeting of diseased cells *in vivo*. Neither of these issues can be addressed apart from in vivo experimentation and the specification does not provide a reasonable expectation of success in overcoming the long-standing and problematic nature of using gene

therapy vectors for treating disease, particularly in view of its highly unpredictable nature. Without any specific working examples in animals, there is no basis for concluding that the instant invention has in fact overcome even one of the many obstacles plaguing successful use of viral vectors for gene therapy. The response further argues that "given the teachings in the present specification, and the knowledge available in the art at the time the present application was filed, any experimentation would not be 'undue', but would merely be routine" (p. 10). However, it is not clear what teachings or "knowledge" Applicant are alluding to. At the time the invention was made, the practice of gene therapy was not routinely performed and was only predictable in being shown not to work as previously set forth by Anderson and Verma. Therefore, the need for working examples and specific guidance is particularly important. However, the specification does not provide *any* specific guidance either for treating HIV infections or genetic diseases. For example, no specific transgenes for genetic diseases or "HIV-inhibiting genes or fragment[s] thereof" are recited. Further, the specification does not teach which diseases can be successfully treated by targeting CD4+ cells, nor do the retroviral vectors overcome limitations in the art concerning gene transfer into non-dividing cells. For example, given the many different types of cells susceptible to HIV, the specification does not provide any reasonable expectation of success, given the broad range of non-dividing, differentiated cells, such as macrophages, that would not be efficiently targeted using the vectors of the instant invention.

The specification teaches that the "present invention offers the following *possibilities*: ... to *develop* gene therapy strategies which require ...., to especially *develop* gene therapy

strategies...etc. etc. (p. 5). The standard for an enabling disclosure is not the *possibility* of *developing* a strategy for gene therapy, but rather a disclosure which provides the guidance and reasonable expectation of success for one of skill in the art to practice the invention commensurate in scope with the claimed subject matter.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed invention. This is particularly true given the state of the art, the nature of the invention, the unpredictability of the art, the scarcity of guidance and working examples in the specification, and the amount of experimentation necessary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 15 and 20 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Schnierle et al. (Proc. Natl. Acad. Sci. USA, 94:8640-8645, 1997) for the reasons set forth against prior claims 1-8 in the Office Action of 3/9/00.

Applicant's arguments filed 9/13/00 have been fully considered but they are not persuasive.

The response argues that the previous rejection made against claims 1-8 should be withdrawn since Applicants have filed a certified translation of German application No. 197707971.7. However, to receive the benefit of an earlier filing date under 35 U.S.C. 119(a), the foreign application must disclose *the same invention* recited in the instant application. In the instant case, claims 15 and 20 recite subject matter not disclosed in German application No. 197707971.7. Since the German application fails to disclose *all* of the specific envelope protein or expression construct embodiments the rejection would still apply to newly amended claims 15 and 20. See MPEP § 201.15.

Claims 13-29 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter for the reasons set forth against prior claims 1-8 in the Office Action of 3/9/00. Applicant's arguments filed 9/13/00 have been fully considered but they are not persuasive. Applicants argue that "although Dr. Schnierle clearly worked on several aspects described in the Schnierle et al. Paper, she did not work on any subject matter that is claimed in the present application" (p. 11). Elsewhere, Applicants contend that "Dr. Schnierle contributed only to specific parts of the 1997 paper, but not to the subject matter that is presently claimed". These contentions are not persuasive, since the response fails to indicate what "equal contribution" Dr. Schnierle actually made with respect to the work disclosed in the Proc. Natl. Acad. Sci. USA reference. Rather than explain the specific contribution that Dr. Schnierle actually made, the response argues that since she was not named as co-author on two additional

journal articles from the same laboratory published after the 1997, "she did not contribute to the presently claimed invention. The fact that Dr. Schnierle was not named as a co-inventor has no probative value in assessing her specific contribution to the 1997 Proc. Natl. Acad. Sci. USA paper which largely overlaps in scope the claimed invention. Using the logic set forth by Applicants, one might be inclined to argue that since co-inventors Cichutek and Stitz are not named as co-authors on the recent MLV/HIV pseudotype paper by Schnierle (Virology, 261(1):70-78, 1999) they are not the rightful inventors on the instant application. Such faulty logic has no place in the instant case. In the absence of any specific details relating to the nature of Dr. Schnierle's "equal contribution" to the work disclosed in the 1997 Proc. Natl. Acad. Sci. USA paper, Applicants have failed to overcome the prima facie case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13-19 and 20-29 are rejected under 35 U.S.C. 103(a) for the reasons set forth against prior claims 1-6 and 8 in the Office Action of 3/9/00 as being unpatentable over Denesvre et al. (J. Virol., 70:4380-4386, 1996) in view of Salmons et al. (Leukemia, 9(Suppl.):S53-S60,

1995) and either Wilk et al. (Virology, 189:167-177, 1992) or Zingler et al. (J. Virol. 67:2824-2831, 1993).

Applicant's arguments filed 9/13/00 have been fully considered but they are not persuasive. Applicants argue that "the combination of Denesvre, Salmons, Wilk, and Zingler fails to provide a reasonable expectation of success of preparing the claimed retroviral vectors or the methods to produce them" (p. 14), that "the combination of Denesvre and Salmons does not render the subject matter of claims 1-6 and 8 obvious"; that Wilk "would put the person of skill in doubt whether incorporation of a truncated HIV transmembrane envelope protein would lead to infectious virions"; that Zingler neither describes or suggest the use of truncated SIV envelope proteins to pseudotype MLV-viral cores; and the "prior art, not applicants' application, must contain the requisite motivation to combine all the cited references" (p. 15). The principal point of Denesvre which was not argued by Applicants, is Denesvre's teaching the "simple rule that retroviral cores allow incorporation of heterologous envelopes whose cytoplasmic tails are smaller than that of the original parental envelope". Since HIV and SIV are retroviruses, this rule would clearly apply to the claimed subject matter of the instant invention, particularly in view of Denesvre's discussion which explicitly discusses the problem of HIV-1 Env containing a long cytoplasmic tail that can not be incorporated into MuLV particles, and through its rule and specific pseudotype examples, implicitly provides a solution to the problem of making MLV/HIV-1 pseudotypes as suggested by Salmons, who clearly provided the motivation to do so. The arguments set forth concerning Wilk and Zingler are not particularly relevant to the instant case.

First, whether or not truncation of the HIV-1 TM has been observed in vivo is immaterial, particularly in view of Applicants clear suggestion that given the ability to target CD4+ cells in vitro "those of skill in this field would expect that the new retroviral vectors would also work ex vivo and in vivo" (p. 10). The fact that Zingler does not suggest use of truncated SIV envelope proteins to pseudotype MLV-viral cores is also not a deficiency given Denesvre's teaching, Salmon's motivation, and the close evolutionary and functional relationship between HIV env and SIV env. If anything, the teachings of Wilk and Zingler support the notion that combining the references of Denesvre, Salmons, Wilk, and Zingler would produce a reasonable expectation of success. Although these teachings cannot make obvious any of the specific transmembrane truncation mutant *species* disclosed in the instant application, they do make obvious the *genus* of MLV/HIV and MLV/SIV pseudotypes and methods of their use as disclosed in the instant application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Brunovskis whose telephone number is (703) 305-2471. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda can be reached at (703) 305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Patent Analyst, Patsy Zimmerman whose telephone number is (703) 308-8338.

Peter Brunovskis, Ph.D.
Patent Examiner
Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [ ] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [X] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other:

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
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